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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,351	07/31/2003	Oliver Harnack	450117-04465	3470

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EXAMINER	
YU, MELANIE J	
ART UNIT	PAPER NUMBER
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,351	HARNACK ET AL.	
	Examiner	Art Unit	
	Melanie Yu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's appeal brief filed 22 September 2006 has been entered and considered. Previous rejections of the claims under 35 USC 103(a) have been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 2-11, 14-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398).

Regarding claims 2, 3 and 14-18 Ford et al. teach a method of attaching a hydrophilic species to hydrophilic macromolecules immobilized on a surface, comprising the steps: providing a surface (par. 0019; par. 0078; par. 0082); immobilizing hydrophilic nucleic acids (hydrophilic macromolecules) on the surface (par. 0019; par. 0078; par. 0082); and exposing the nucleic acids immobilized on the surface to metal complexes (par. 0079) of gold nanoparticles (a hydrophilic species, par. 0010), whereby the hydrophilic

species are attached to the hydrophilic macromolecules (metallization of DNA shows metal particle attachment of DNA, par. 0079), and wherein the nucleic acid is DNA (par. 0020) and is double-stranded or single-stranded (par. 0020). Ford et al. fail to teach the surface being hydrophobic.

Klein et al. teach a hydrophobic substrate (polystyrene coated silicon, pg. 2396, right column, second paragraph) having a nucleic acid immobilized directly to the polystyrene surface (one end of the DNA binds to polystyrene, pg. 2396, right column, second paragraph), in order to provide an attachment method that is highly parallel.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al., attachment of one end of nucleic acids on a hydrophobic surface as taught by Klein et al., in order to provide an attachment method that is easy to employ and results in high yield.

With respect to claims 4 and 11, Ford et al. teach the hydrophilic species in a water solution (par. 0023).

Regarding claims 5, 6 and 20, Ford et al. teach an additional step of growing an attached hydrophilic species to a larger size and wherein the attached hydrophilic species is exposed to an electroless plating solution (enlargement of particles by electroless deposition, par. 0010). Ford et al. further teach the electroless plating solution (par. 0011; par. 0030) comprising a gold salt and a reducing agent (solution contains metal ion species of Au and reducing reagent, par. 0011).

With respect to claims 7-10, Klein et al. teach immobilizing the hydrophilic macromolecules on the surface by applying the hydrophilic macromolecules to the surface by dip-coating (pg. 2396, right column, second paragraph). Ford et al. teach exposing the hydrophilic macromolecules to the species for 10 minutes (par. 0079), which is

encompassed by the recited ranges of between 1 second and 20 minutes and between 10 seconds and 10 minutes. Wherein the surface is hydrophobic as taught by Klein et al.

3. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398) in light of Tajima et al. (US 4,649,071).

Ford et al. in view of Klein et al. teach a hydrophobic substrate being polystyrene, but fail to teach the specific water contact angle properties of polystyrene. However, Tajima et al. teach that an untreated polystyrene surface has water contact angle of 85° (example 5), which is encompassed by the recited ranges of from 30° to 110° and 60° to 110°.

4. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398), as applied to claim 2, further in view of Berning et al. (^{198}Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals, 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583).

Ford et al. in view of Klein et al. teach a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, but fail to teach the hydrophilic species being tris(hydroxymethyl)phosphine-gold nanoparticles.

Berning et al. teach a hydrophilic species of tris(hydroxymethyl)phosphine-gold nanoparticles (581, Discussion, 1st paragraph), in order to evaluate their potential utility in the design of Au(I)-containing drugs.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al. in view of Klein et al., a

tris(hydroxymethyl)phosphine-gold nanoparticle as taught by Berning et al., in order to provide metal complexes that exhibit *in vitro* stability.

5. Claims 2-11, 14-16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220).

Regarding claims 2, 3 and 14-18 Ford et al. teach a method of attaching a hydrophilic species to hydrophilic macromolecules immobilized on a surface, comprising the steps: providing a surface (par. 0019; par. 0078; par. 0082); immobilizing hydrophilic nucleic acids (hydrophilic macromolecules) on the surface (par. 0019; par. 0078; par. 0082); and exposing the nucleic acids immobilized on the surface to metal complexes (par. 0079) of gold nanoparticles (a hydrophilic species, par. 0010), whereby the hydrophilic species are attached to the hydrophilic macromolecules (metallization of DNA shows metal particle attachment of DNA, par. 0079), and wherein the nucleic acid is DNA (par. 0020) and is double-stranded or single-stranded (par. 0020). Ford et al. fail to teach the surface being hydrophobic.

Schueller et al. teach a hydrophobic substrate (polystyrene, par. 68) having a biological molecule immobilized directly to the polystyrene surface (biological molecules stamped directly onto a polystyrene surface, par. 68; biological molecule may be a protein or nucleic acid, par. 68), in order to provide an improved method for stamping materials on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al., nucleic acids directly onto a hydrophobic surface as taught by Schueller et al., in order to provide a method for attachment of molecules that is more efficiently processed.

With respect to claims 4 and 11, Ford et al. teach the hydrophilic species in a water solution (par. 0023).

Regarding claims 5, 6 and 20, Ford et al. teach an additional step of growing an attached hydrophilic species to a larger size and wherein the attached hydrophilic species is exposed to an electroless plating solution (enlargement of particles by electroless deposition, par. 0010). Ford et al. further teach the electroless plating solution (par. 0011; par. 0030) comprising a gold salt and a reducing agent (solution contains metal ion species of Au and reducing reagent, par. 0011).

With respect to claims 7-10, Ford et al. teach immobilizing the hydrophilic macromolecules on the surface by applying the hydrophilic macromolecules to the surface (par. 0078) by spin-coating (par. 0078). Ford et al. further teach exposing the hydrophilic macromolecules to the species for 10 minutes (par. 0079), which is encompassed by the recited ranges of between 1 second and 20 minutes and between 10 seconds and 10 minutes. Wherein the surface is hydrophobic as taught by Schueller et al.

6. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220) in light of Tajima et al. (US 4,649,071).

Ford et al. in view of Schueller et al. teach a hydrophobic substrate being polystyrene, but fail to teach the specific water contact angle properties of polystyrene. However, Tajima et al. teach that an untreated polystyrene surface has water contact angle of 85° (example 5), which is encompassed by the recited ranges of from 30° to 110° and 60° to 110°.

7. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220), as applied to claim 2, further in view of Berning et al. (^{198}Au-Labeled Hydroxymethyl Phosphines as Models for

Potential Therapeutic Pharmaceuticals, 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583).

Ford et al. in view of Schueller et al. teach a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, but fail to teach the hydrophilic species being tris(hydroxymethyl)phosphine-gold nanoparticles.

Berning et al. teach a hydrophilic species of tris(hydroxymethyl)phosphine-gold nanoparticles (581, Discussion, 1st paragraph), in order to evaluate their potential utility in the design of Au(I)-containing drugs.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al. in view of Schueller et al., a tris(hydroxymethyl)phosphine-gold nanoparticle as taught by Berning et al., in order to provide metal complexes that exhibit *in vitro* stability.

Double Patenting

8. Claims 2-6, 11, 15 and 17-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 14 and 15 of copending Application No. 10/210812 in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398). Claims 1 and 2 of application '812 recite a hydrophilic macromolecule (nucleic acid) exposed to a hydrophilic nanospecies (trips(hydroxymethyl)phosphine-Au) and the complex immobilized on a substrate. However, application '812 fails to recite a hydrophobic substrate. Klein et al. teach immobilization of one end of a nucleic acid on a hydrophobic substrate to provide an attachment method that is highly parallel. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of application '812, attachment of one end of a nucleic acid on a hydrophobic substrate as

taught by Klein et al., in order to provide an attachment method that is easy to employ and results in high yield. Claims 3, 4, 5, 14 and 15 of application '812 recite a hydrophilic species in a water solution, the species grown to a larger size with an electroless plating solution, and the metal for the nanospecies being Au. Claim 4 recites the nucleic acid being single or double stranded.

9. Claims 2-6, 11, 15 and 17-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 14-16 and 20 of copending Application No. 09/990,049 in view of Caldwell et al. (US 5,516,703). Claims 1, 2 and16 of application '049 recite a hydrophilic macromolecule (nucleic acid) exposed to a hydrophilic nanospecies (metal complex) and the complex immobilized on a substrate. However, application '049 fails to recite a hydrophobic substrate. Klein et al. teach immobilization of one end of a nucleic acid on a hydrophobic substrate to provide an attachment method that is highly parallel. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of application '049, attachment of one end of a nucleic acid on a hydrophobic substrate as taught by Klein et al., in order to provide an attachment method that is easy to employ and results in high yield. Claims 2-4, 14-16 and 20 of application '049 recite a hydrophilic species in a water solution, the species grown to a larger size with an electroless plating solution, and the metal for the nanospecies being Au. Claim 4 recites the nucleic acid being single or double stranded.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

10. Applicant's arguments with respect to claims 2-20 have been considered but are moot in view of the new ground(s) of rejection. The previous rejections of the claims have been withdrawn. However, upon further consideration, a new ground(s) of rejection is

made in view of the teachings of Klein et al. wherein one end of nucleic acids are attached to a hydrophobic polystyrene surface.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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